

REMARKS/ARGUMENTS

Applicants submit the aforementioned amendments and following remarks in response to the Office Action mailed June 30, 2008.

A petition for a two-month extension is herewith requested.

Claims 2 and 5 are pending. Claims 2 and 5 have been amended. Support for the amendment may be found throughout the application as originally filed, for example, paragraphs [0005] and [0017]. No new matter is added.

Reconsideration is respectfully requested in view of the above amendments and the following remarks.

Claim Objection

Claim 2 was objected as containing typographic error.

Claim 2 is amended as suggested by the Examiner. Accordingly, the objection is obviated.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 2 and 5 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite.

Claims 2 and 5 are amended to specify the wild-type residue of glutamate at position 194 as suggested by the Examiner. Accordingly, the rejection under 35 U.S.C. § 112, second paragraph, is obviated.

Rejection under 35 U.S.C. § 103(a)

Claims 2 and 5 are rejected under 35 U.S.C. § 103(a) over Stein et al. 1994 in view of GenBank data/Servais et al. 2001 and Kim et al. 2001. The Examiner states that Stein et al. and Servais et al. disclose drug-resistance mutation profiles contributed by a reverse transcriptase inhibitor (RTI) AZT and that Kim et al. discloses an assay of introducing a RTI to a sample containing resistant mutations to identify potent PRI.

Applicants have amended claims 2 and 5 to recite the method for evaluating the an HIV RTI for a second anti-HIV therapy comprising receiving a sample from an HIV-infected patient treated with a first anti-HIV therapy; determining whether said sample from said HIV-infected patient comprises a nucleic acid encoding HIV reverse transcriptase having at least one mutation at the position 194, wherein the wild type amino acid glutamate is mutated to glycine

(E194G) as compared to the wild-type HIV strain IIIB/LAI; introducing said HIV reverse transcriptase inhibitor for said second anti-HIV therapy to said sample from said HIV-infected patient containing said mutation; comparing the effectiveness of said inhibitor in said sample containing said reverse transcriptase mutation, with a sample containing no such said mutation; and correlating the presence of said at least one mutation of step (ii) to a change in effectiveness of said HIV reverse transcriptase inhibitor.

Applicants respectfully submit that none of the cited documents, alone or in combination, discloses or suggests the claimed methods as currently amended.

Stein et al. discloses 21 different substitutions in proviral reverse transcriptases isolated from the patients being treated with nothing else but AZT. Stein et al. focuses on some of the 21 mutations and their effect on resistance only to AZT. Clearly, Stein et al. does not disclose or suggest the use of reverse transcriptase mutation for evaluating any other HIV RTI. Further, Stein et al. does not disclose or suggest the use of HIV RTI for a second anti-HIV therapy. Therefore, Stein et al. does not disclose each and every element of claims 2 and 5.

The data sheet of GenBank CAB86592 contains the protein sequence of accession AJ401823.1 for HIV-1 isolate 98371. The data sheet only discloses HIV-1 isolate 98371 has glycine at position 194 in reverse transcriptase. The data sheet does not disclose or suggest the use of E194G mutation for evaluating HIV RTI nor the use of HIV RTI for a second anti-HIV therapy. Accordingly, the deficiency in Stein et al. cannot be cured by GenBank CAB86592.

With regard to Servais et al. 2001 referred in GenBank CAB86592, Applicants have reviewed the article multiple times and are not able to locate the E194G mutation, accession number AJ401823.1 nor isolate 98371. Servais et al. discloses the sequences, with accession numbers AJ 3213, 10414-17, 10488-90, 11401-07, and 401723-1977, isolated from 26 patients being treated with combination drugs of two RTI and one protease inhibitor. Therefore, Servais et al. discloses mutations derived from both RTI and protease inhibitor. Servais et al. does not disclose the E194G mutation, any use thereof, or the use of HIV RTI for a second anti-HIV therapy. Accordingly, the deficiency in Stein et al. cannot be cured by Servais et al.

Kim et al. discloses effect of FLT or AZT on the PBMC cell line, not a sample from a patient, infected by HIV-1 isolates containing various mutations in reverse transcriptase. Further, Kim et al. does not disclose or suggest the E194G mutation, any use thereof, or the use of HIV RTI for a second anti-HIV therapy. Accordingly, the deficiency in Stein et al. cannot be cured by Kim et al.

To establish a *prima facie* case of obviousness, the cited references when combined must disclose each and every element of the claim. See MPEP § 2143. None of Stein et al., GenBank data, Servais et al. or Kim et al., alone or in combination, discloses each and every element of the claim as presently amended. Further, there is no suggestion or motivation in any of the cited documents, nor a person skilled in the art will find any reason, to combine the cited documents and use the E194G mutation as recited in the amended claims.

Accordingly, claims 2 and 5 as amended are not obvious in view of the cited documents. Reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a) are respectfully requested.

In view of the foregoing amendment and remarks, allowance of claims 2 and 5 is respectfully requested.

Applicants respectfully request that a timely Notice of Allowance be issued in this case.

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Respectfully submitted,

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